Non-Technical Abstract

Bone cancers (referred to medically as osteosarcomas or osteogenic sarcomas) are cancers arising from the bones and occur most frequently during childhood and adolescence. Bone cancer was once fatal in more than 80% of patients. Chemotherapy, better surgical techniques and improved staging methods now allow most patients to be treated without amputation and to be cured of their disease. However, many patients are not cured and die when their cancer spreads to vital organs such as the lungs. The lung is the most frequent site of tumor spread and is treated with chemotherapy and surgical resections. Often multiple lung surgeries are required for tumors that continue to come back in the lung. Eventually more surgery can no longer be done because either too much lung tissue has been removed or the surgery has become futile because more tumors quickly reappear. Although a main component of initial therapy, chemotherapy has not been shown to be of benefit for recurrent disease.

This trial uses a virus based on a human-type adenovirus to specifically target and kill bone cancer that has spread to the lungs. The Ad-OC-E1a virus (OCaPl) has been altered to restrict the spread of the virus to bone cancers. Upon injection of Ad-OC-E1a into the vein the virus will go first to the lung where we hope it will kill the bone cancer cells there while leaving the normal tissues unharmed. The ability to specifically target bone cancer cells comes from the placement of a control element of DNA (the osteocalcin promoter) that functions in cells that have the ability to deposit calcium such as some normal bone cells and bone cancers. Normally the osteocalcin promoter is primarily active during development, when bones are growing. Bone cancer cells have properties similar to growing bones, which makes them particularly sensitive to the osteocalcin promoter. Bone cancer cells often keep these properties even if they have spread to other sites, such as the lung. Therefore, this study hopes to demonstrate the ability of Ad-OC-E1a to safely target and kill bone cancer cells by using a cancer-specific control element (osteocalcin promoter) that prevents the spread of the virus to normal tissues while allowing it remain active in cancer cells.

This study will study Ad-OC-E1a for the treatment of metastatic cancer that can no longer be cured with chemotherapy. In the first part of the study subjects will receive a single intravenous injection with one of four doses of Ad-OC-E1a. Once safety is established in this part of the study, we will then determine the anti-tumor activity of Ad-OC-E1a in subjects with bone cancer that has spread to the lungs for whom an operation to remove the lung tumors is indicated as part of their standard care. To determine if Ad-OC-E1a is active in these subjects, they will have CT scans of their lungs and surgical removal of their lung tumors.